



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/799,369

03/12/2004

Elena V. Bolchakova

1560.002US1

6361

22896 7590 01/10/2008
MILA KASAN, PATENT DEPT.
APPLIED BIOSYSTEMS
850 LINCOLN CENTRE DRIVE
FOSTER CITY, CA 94404

EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

01/10/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|-------------------------------|-----------------------------------|--|
| Office Action Summary | Application No. 10/799,369 | Applicant(s) BOLCHAKOVA ET AL. | |
| | Examiner Richard G. Hutson | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/23/2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 1-33, 37-40, 44, 45 and 47-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34 and 35 is/are rejected.
- 7) ☒ Claim(s) 36 and 41-43 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants amendment of claim 34, in the paper filed on 7/13/2007 and 10/23/2007, are acknowledged. Claims 1-55 are still at issue and are present for examination. Claims 1-22 are still at issue and are present for examination.

Applicants' arguments filed on 7/13/2007 and 10/23/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 1-33, 37-40, 44, 45 and 47-55 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure was previously objected to because of the following informalities:

Applicant's specification states that SEQ ID NO: 22 has Tyr in place of Phe at position 668 and shows the corresponding "Y" underlined on page 57, line 7. This numbering of the amino acid residues of SEQ ID NO: 22 on page 57 does not correspond to applicant's disclosure of SEQ ID NO: 22 in the sequence listing. For example the corresponding underlined "Y" residue of page 57, is listed as Tyr residue 665 in the sequence listing, even though the description of SEQ ID NO: 22, in the sequence listing states that "Tyr is used in place of the Phe at position 668".

In response applicants have stated that the discrepancy arises because of the alignment of the amino acid sequence with the position numbering in the sequence

listing, however it appears that the discrepancy arises because of amino sequence numbering in applicants specification at page 56-57.

Appropriate correction or explanation is required.

Claim Objections

Claim 34, 35, 36, 41-43 and 46 are objected to because of the following informalities:

Claim 34 recites "polymeras". This should be "polymeraseis".

Claim 35 remains objected to because it is drawn to the nucleic acid polymerase of claim 34, when claim 34 is drawn to a "DNA polymerase polypeptide". In response to this previous objection, applicants stated that they cancelled claim 35, however, claim 35 still exists.

Claim 46 is objected to because it depends from non-elected claim 44.

Claims 36, 41-43 contain non-elected subject matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 36, 41-43 and 46 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention is withdrawn based upon the explanation of SEQ ID NO: 22 presented by applicants. It is noted, however, that while this rejection is withdrawn, the previous objection to the specification is maintained as discussed above.

Claims 34 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA polymerase having the amino acid sequence of SEQ ID NO: 22 and having DNA polymerase activity, does not reasonably provide enablement for any DNA polymerase polypeptide from *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 34, and 36. In response to this rejection applicants have amended claim 34 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection together with the rejection under written description on the basis that ATCC deposit 27978 contains *Thermus scotoductus* strain X-1 and the polymerase of claim 34 is the polymerase naturally encoded by the deposited strain as well as obvious variants thereof. Applicants also note that claim 46 has been cancelled, however, this does not appear to be true.

Applicant's complete argument is acknowledged and has been carefully considered, however, is not found persuasive on the basis that claims 34 and 46

continue to be so broad as to encompass any DNA polymerase "polypeptide" from *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978 or any polymerase made by the method of claim 44. While it acknowledged that the *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978 is publically available, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims, including "any DNA polymerase polypeptide" from *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978 having an undefined activity. The claims rejected under this section of U.S.C. 112, first paragraph, do not place any functional limits on the claimed polypeptides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that DNA polymerase polypeptide from *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978 having the amino acid sequence of SEQ ID NO: 22 and having DNA polymerase activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the

desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polymerase polypeptide from *Thermus scotoductus* strain X-1, ATCC Deposit No. 27978, because the specification does not establish: (A) regions of the polypeptide structure which may be modified without effecting polymerase or desired activity; (B) the general tolerance of polymerase polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a polymerase polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired or required activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having an undefined activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any polymerase polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gelfand et al. (U.S. 6,228,628, issued 5/2001).

Gelfand et al. teaches methods for isolating DNAs that encode DNA polymerases and further teaches that DNA polymerase genes can be recovered from *Thermus* species ATCC Deposit No. 27978 (see sentence bridging columns 15-16). And one of skill in the art would have found it *prima facie* obvious to isolate a nucleic acid encoding a polymerase as well as the polymerase itself from this strain

Gelfand et al. teach the motivation to isolate the claimed nucleic acids and polymerases and further teach examples of such showing that the expectation of success was high.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Richard G Hutson, Ph.D.
Primary Examiner

Application/Control Number:
10/799,369
Art Unit: 1652

Page 9

Art Unit 1652

rg
1/2/2008